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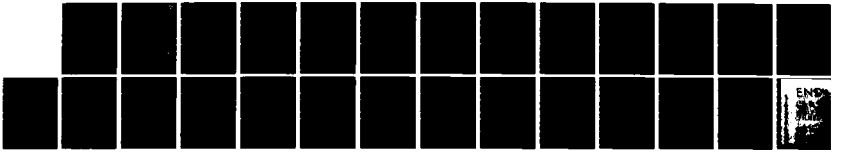

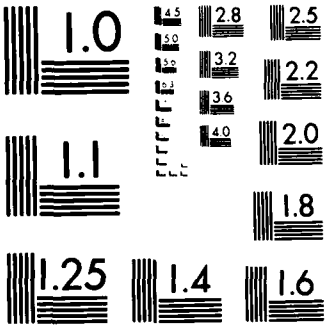

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In awake goats before and after ablation of carotid bodies (CBx) we studied the effect of acute metabolic acidosis (AMA) produced by intravenous infusion of HCl on composition of arterial blood and CSF, and on ventilatory responsiveness to hyperoxic CO_2 rebreathing. AMA caused decrease in $PaCO_2$ (breathing air at rest) indicating that alveolar ventilation was increased relative to CO_2 production; position of CO_2 response curves was shifted toward lower values of PCO_2. These changes were similar before and after CBx, though the levels of PCO_2 in arterial blood during air breathing at rest, and in expired gas at a

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given level of ventilation during CO_2 rebreathing, were higher after CBx. We conclude that a respiratory adaptation to AMA does occur in goats deprived of peripheral chemoreceptors, and is probably mediated by the central chemoreceptors.

RESPIRATION OF CHEMODENERVATED GOATS

IN ACUTE METABOLIC ACIDOSIS

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ABSTRACT

In awake goats before and after ablation of carotid bodies (CBx) we studied the effect of acute metabolic acidosis (AMA) produced by intravenous infusion of HCl on composition of arterial blood and CSF, and on ventilatory responsiveness to hyperoxic CO_2 rebreathing. AMA caused decrease in $PaCO_2$ (breathing air at rest) indicating that alveolar ventilation was increased relative to CO_2 production; position of CO_2 response curves was shifted toward lower values of PCO_2. These changes were similar before and after CBx, though the levels of PCO_2 in arterial blood during air breathing at rest, and in expired gas at a given level of ventilation during CO_2 rebreathing, were higher after CBx. We conclude that a respiratory adaptation to AMA does occur in goats deprived of peripheral chemoreceptors, and is probably mediated by the central chemoreceptors.

Key words: carotid bodies, CO_2 rebreathing, CSF

INTRODUCTION

Acid-base disturbances of primarily "metabolic" origin elicit respiratory compensation. In metabolic (hyperchloremic) acidosis, $PaCO_2$ is lowered, which alleviates the acidemia. An opposite change in $PaCO_2$ occurs in primary hypochloremic (metabolic) alkalosis. Furthermore, the ventilatory responses to increase in $PaCO_2$ produced by CO_2 inhalation are shifted to lower values of $PaCO_2$ in the presence of metabolic acidosis, and to higher $PaCO_2$ values in metabolic alkalosis (Fencl et al. [1966]). The roles played by the carotid bodies (CB) and by the central chemoreceptors in these respiratory adaptations are disputed. A predominant role was ascribed to central chemoreceptors by Fencl et al. [1966], and Pappenheimer [1967], while Mitchell [1965] and Bainton [1978] concluded from their studies in awake dogs that excision of CB (CBx) abolishes the respiratory response to primary metabolic acid-base disturbances. More recently, Javaheri et al. [1979] and Kaehny and Jackson [1979] reported that in dogs, metabolic acidosis does stimulate ventilation in the absence of CB.

In awake goats before and after CBx, we studied the effect of acute metabolic acidosis (AMA) on composition of arterial blood and CSF, and on responsiveness to CO_2 rebreathing. A respiratory adaptation to AMA did occur in goats deprived of CB function. As before chemodenervation, it was manifested by decrease in the resting $PaCO_2$ and by a shift of the CO_2 response curves to lower PCO_2 values.

METHODS

General

The studies were performed in four awake goats weighing 36-44 kg

(mean 40 kg), surgically prepared with carotid loops and with implanted occipital guide tubes for sampling cisternal CSF. The same animals were used in another study (Steinbrook et al. [1983]).

On each experimental day we punctured the cistern through the guide tube, percutaneously inserted a plastic cannula into the carotid artery in the loop and inserted another into the superior vena cava through the contralateral external jugular vein. Carotid arterial blood pressure was continuously monitored with a transducer (Statham 23DB). We sampled cisternal CSF and arterial blood while the goats inhaled room air. The arterial blood sample was obtained when a steady state in gas exchange was apparent from stability of end-tidal PCO_2. Next we measured the ventilatory response to hyperoxic CO_2 rebreathing. We then induced AMA by infusing 0.2 N HCl in isotonic saline into the superior vena cava. The total dose of HCl was 30 mmol/kg of body weight, delivered over approximately one hour at a steady rate, unless there was indication for slowing the rate, such as occasional extrasystoles or bradycardia observed in some animals during the first minutes of infusion. The goats appeared calm during the infusion. Fifteen to twenty minutes after completion of the infusion, we repeated sampling of cisternal CSF and arterial blood, and CO_2 rebreathing. Each animal was studied twice before and twice four to five weeks after CBx. Means of the two measurements in each condition were used for data analysis.

CB were ablated under general anesthesia, by excision and by applying to denuded arterial walls a saturated solution of phenol in 95% alcohol, as previously described (Steinbrook et al. [1983]). Completeness of the chemodenervation was tested by measuring the ventilatory response of

awake animals to acute hypoxia and to injection of cyanide (1 μmol/kg BW), before CBx and 3-5 weeks after operation (approximately 1 week before the first post-denervation respiratory measurements). We have documented in a previous publication (Steinbrook et al. [1983]) that the goats used in the present study were deprived of peripheral chemoreception after CBx.

Respiratory Measurements

The techniques have previously been described in detail (Steinbrook et al. [1983]). In brief, the goats wore latex rubber masks and breathed through a low resistance non-rebreathing valve (J-valve, Model P-307, dead space 92 ml, Warren E. Collins). Volume of expired gas was measured with a Wedge spirometer (Med-Science Electronics). Concentrations of CO_2 and O_2 at the airway were measured with an infrared analyzer (Beckman LB-2), and mass spectrometer (Perkin Elmer, MGA 1100A). All measured variables were recorded on a strip chart (Gould Brush Model 200), and on a magnetic tape (Hewlett Packard Model 3968).

For hyperoxic CO_2 rebreathing, a modification of Read's technique [1967] was used (Steinbrook et al. [1983]). Linear regressions were derived for minute ventilation (on a breath-by-breath basis) as a function of the simultaneously measured end-tidal PCO_2 ($P_{ET}CO_2$). Ventilatory responsiveness to CO_2 was compared using slopes of these regressions and values of $\dot{V}_E$ at $P_{ET}CO_2$ = 60 torr.

Analytical Techniques

Radiometer electrodes and electronics (BMS3 MK2) were used to measure PCO_2, PO_2 and pH in arterial blood and CSF at 37°C with correction to

rectal temperature (Mitchell et al. [1965], Gabel [1980]). CO_2 concentration (C_{CO_2}) in CSF was measured with a Natelson microgasometer (Scientific Industries), and [Cl^-] in anaerobically separated plasma and in CSF by potentiometric titration (Aminco-Cotlove, American Instruments). Bicarbonate in plasma and in CSF was calculated from measured pH and P_{CO_2} or C_{CO_2}, applying published values for pK' and CO_2 solubilities (Mitchell et al. [1965]). Base excess (BE) was determined with a Blood Gas Calculator (Severinghaus [1966]).

Statistical Analyses

Student's t-test, analysis of variance, or a non-parametric test of variance (Conover [1971]) was applied, as indicated.

RESULTS

The effect of CBx and AMA on the composition of arterial blood and CSF, are shown in table 1. CBx produced a mild respiratory acidosis with statistically significant hypercapnia, acidemia, and hypoxemia; in CSF, no significant changes occurred in the mean values of P_{CO_2} and pH. The standard infusion of HCl produced an AMA of similar severity before and after CBx. The mean (± S.E.) change in BE during AMA was -9.1 ± 0.8 and -7.7 ± 0.9 meq/L in intact and chemodenervated goats, respectively (not different by t-test for paired samples or by ranking test of variance). Mean values of BE, [Cl^-] and [HCO_3^-] in arterial blood plasma during AMA were similar before and after CBx (table 1).

Table 1

In spite of the resting hypercapnia observed after CBx during normal metabolic acid-base balance, Pa_{CO_2} decreased in response to AMA after CBx, as it did before chemodenervation. When CB were intact, AMA caused

reduction in mean $PaCO_2$ from 37.1 to 33.0 torr ($p < 0.05$). Mean (± S.E.) change in $PaCO_2$ response to AMA was -3.4 ± 0.7 torr in intact goats; after chemodenervation, it was -4.0 ± 1.4 torr. The mean (± S.E.) decrease in $PaCO_2$ per unit of acute base deficit ($\Delta PaCO_2/\Delta BE$) was 0.37 ± 0.07 torr $(meq/L)^{-1}$ before CBx, and 0.53 ± 0.17 torr $(meq/L)^{-1}$ after chemodenervation ($p < 0.05$, by ranking test of variance). Thus the hyperventilation elicited by AMA was not less after CBx, and it appeared even somewhat more pronounced with ablated CB.

In CSF, mean PCO_2 was the same before and after CBx when the goats were in normal metabolic acid-base balance (table 1). AMA caused a decrease in CSF PCO_2 both before and after CBx, but the mean (± S.E.) change was smaller after CBx than before (-3.3 ± 0.7 and -5.0 ± 1.2 torr, respectively; $p < 0.05$, ranking test of variance). Thus, during AMA, mean CSF PCO_2 was higher after CBx than before (41.6 vs 38.8 torr). In both conditions, a small increase in mean $[Cl^-]$ was manifest in CSF during AMA, with reciprocal change in $[HCO_3^-]$ ($p < 0.05$). CSF pH did not change with AMA before or after CBx.

During normal acid-base balance, the mean (± S.E.) difference between PCO_2 in CSF and in arterial blood ($P_{csf}CO_2 - PaCO_2$) was 7.0 ± 1.0 and 4.9 ± 0.3 torr ($p < 0.05$) before and after CBx, respectively. In response to AMA, this difference was reduced when CB were intact (fig. 1), on the

Figure 1

average by -1.8 ± 0.8 torr. In contrast, with CB ablated, ($P_{csf}CO_2 - PaCO_2$) increased in response to AMA in 3 of 4 observations, on the average by +1.5 ± 0.9 torr. These changes in ($P_{csf}CO_2 - PaCO_2$) during AMA in intact and chemodenervated goats are statistically different ($p < 0.05$ by t-test for paired samples).

Data on hyperoxic CO_2 rebreathing are summarized in table 2 and fig. 2. In the normal metabolic acid-base balance, CBx produced a statistically significant ($p < 0.01$) shift of the CO_2 response curves to higher $P_{ET}CO_2$ values, as indicated by a decrease in the value of $\dot{V}_E$ at $P_{ET}CO_2$ = 60 torr. However, the slopes of the curves were not significantly different. AMA produced a change in the ventilatory response to CO_2 that was similar before and after CBx. Slopes of the curves did not change significantly with AMA either before or after CBx, but in both conditions, AMA caused a statistically significant increase in the mean values of $\dot{V}_E$ at $P_{ET}CO_2$ = 60 torr, indicating that position of the CO_2 response curves was shifted to lower $P_{ET}CO_2$ values.

Table 2

Figure 2

DISCUSSION

We have presented evidence in a previous communication (Steinbrook et al. [1983]) that the goats used in the present study were deprived of peripheral chemoreception after CBx: the ventilatory response to hypoxia of 5-10 minutes duration was abolished, and during hyperoxia (PaO_2 > 300 torr for 5-10 minutes), pulmonary ventilation was increased; stimulation of ventilation by acute hyperoxia typically occurs in chemodenervated animals (Davenport et al. [1947], Miller and Tenney [1975]).

After CBx, while breathing air at rest, the goats in normal acid-base balance were mildly hypercapnic. However, starting from these higher baseline $PaCO_2$ values, chemodenervated goats lowered their resting $PaCO_2$ in response to AMA, just as they did when the CB were intact. The degree of lowering of $PaCO_2$ in relation to base deficit in blood was even greater after CBx. Thus, a ventilatory response to AMA was manifest in the

chemodenervated awake goats. This is in agreement with findings in anesthetized cats (Katsaros [1965]) and in dogs, both anesthetized (Javaheri et al. [1979]) and awake (Kaehny and Jackson [1979]). Our findings are at variance with those of Mitchell [1965] and of Bainton [1978] in awake dogs. In the experiments of Mitchell and Bainton, the degree of hyperchloremic acidosis was much smaller than in our goats. In Mitchell's data, the mean base deficit was about 3 meq/L (estimated from data in table 2, p. 120, l.c.). Bainton administered about 1.5 mmol of HCl per kg of body weight (compared to our dose of 30 mmol/kg, which resulted in a base deficit of 9 to 10 meq/L). In our results, CO_2 response curves were shifted to higher PCO_2 values after CBx. This is in agreement with the findings of Tenney and Brooks [1966] in awake goats. However, induction of AMA displaced the CO_2 response curves to lower PCO_2 values, both before and after CBx. Similar results were obtained in anesthetized cats by Katsaros [1965]. It appears that a respiratory adaptation to AMA, manifest in lowering the resting $PaCO_2$ and in shifting CO_2 response curves to lower PCO_2 values, did occur in our awake goats with ablated CB.

The question arises whether the observed respiratory adaptation to AMA could be mediated by the central chemoreceptors, as postulated for stable metabolic acidosis (Pappenheimer [1967]). The stimulus for the central chemoreceptors is believed to be increase in $[H^+]$ in the cerebral interstitial fluid (cISF) that surrounds the receptors (Mitchell et al. [1963], Fencl et al. [1966]). In stable metabolic acid-base disturbances of several days' duration, $[H^+]$ in cisternal CSF appears to approximate $[H^+]$ in cISF (Fencl et al. [1966]). However, during acutely developing metabolic acidosis, a "paradoxical" alkaline shift in CSF pH can be seen in spontaneously breathing anim ls (Robin et al. [1958]). This results

from the high permeability of the blood-brain barrier for CO_2 on one hand, and the low permeability of the blood-CSF barrier for ions on the other. As ventilation is stimulated by the metabolic acidosis, PCO_2 in brain tissue and in cisternal CSF decreases before any change in CSF $[HCO_3^-]$ occurs.

We sampled CSF about 1 hour after termination of HCl infusion. PCO_2 in CSF was lowered at that time, both before and after CBx; however, we did not observe an alkaline shift in CSF pH. There was an indication that $[HCO_3^-]$ had already begun to decrease and $[Cl^-]$ to increase in CSF at the time of sampling. In such transient states, large-cavity CSF does not reflect the composition of cISF (Fencl et al. [1977], Javaheri et al. [1981], Loeschcke and Ahmad [1982]). In experiments in which pH was measured by electrodes attached to brain surface, and cerebral-tissue PCO_2 derived from measured PCO_2 values in arterial and sagittal sinus blood (Pontén and Siesjö [1966]), it was found that in the fluid underlying the pH electrode (which presumably approximates cISF), $[H^+]$ increased and $[HCO_3^-]$ decreased within minutes after induction of acute metabolic acidosis in blood, before any change in $[HCO_3^-]$ in cisternal CSF was detected (Fencl et al. [1977], Javaheri et al. [1981]). Thus, changes in the ionic composition of cISF, in response to acute systemic acid-base disturbances, seem to precede those in large-cavity CSF. It is thus possible that stimulation of central chemoreceptors by increased $[H^+]$ in cISF plays a role in respiratory adaptations to AMA (Javaheri et al. [1979]) similar to that proposed for stable acid-base disturbances (Pappenheimer [1967]).

PCO_2 in cisternal CSF approximates the cerebral tissue PCO_2 (Pontén and Siesjö [1966]). The difference between cisternal CSF PCO_2 and $PaCO_2$

(ΔPCO_2) is mainly a function of cerebral blood flow (in relation to cerebral CO_2 production). While CB were intact, this ΔPCO_2 was reduced during AMA, suggesting a (relative) increase in cerebral blood flow. This was similar to findings in awake dogs (Chazan et al. [1969]) and in humans (Fencl et al. [1969]) in metabolic acidosis. However, after CBx, the mean ΔPCO_2 increased with AMA. This may suggest that the regulation of cerebral blood flow in response to AMA was changed after CBx. Cerebral vasodilation in response to hypercapnia and hypoxia was found to be reduced in anesthetized animals after CBx (Ponte and Purves [1974]); this was not confirmed in another study (Bates and Sundt [1976]). Vatner et al. [1980] have shown that cerebral vascular responses to stimulation of peripheral chemoreceptors and baroreceptors can be altered by general anesthesia. Measurements of cerebral blood flow in intact and chemodenervated awake animals are needed to determine whether CB have any role in the regulation of cerebral blood flow (and therefore of cerebral-tissue PCO_2) in response to acid-base disturbances.

In chemodenervated goats, the values of PCO_2 in arterial blood while breathing air, and P_{ETCO_2} values at a given $\dot{V}_E$ during CO_2 rebreathing, were higher than before CBx, both before and during AMA. Nonetheless, the changes in these PCO_2 values produced by AMA were similar before and after CBx. Perhaps in the regulation of these responses, the input from CB influences the set point, while gain of the controller reflects input from the central chemoreceptors.

Footnote (on front page)

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In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care", as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory and Animal Resources, National Academy of Sciences, National Research Council.

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References

Bainton, C.R. (1978). Canine ventilation after acid-base infusions, exercise, and carotid body denervation. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 44: 28-35.

Bates, D. and T.M. Sundt, Jr. (1976). The relevance of peripheral baroreceptors and chemoreceptors to regulation of cerebral blood flow in the cat. Circulation Res. 38: 488-493.

Chazan, J.A., F.M. Appleton, A.M. London and W.B. Schwartz (1969). Effects of chronic metabolic acid-base disturbances on the composition of cerebrospinal fluid in the dog. Clin. Sci. 36: 345-358.

Conover, W.J. (1971). Practical Nonparametric Statistics. New York: J. Wiley & Sons, pp. 223-236.

Davenport, H.W., G. Brewer, A.F. Chambers and S. Goldschmidt (1947). The respiratory responses to anoxemia of unanesthetized dogs with chronically denervated aortic and carotid chemoreceptors and their causes. Am. J. Physiol. 148: 406-416.

Fencl, V., J.R. Dmochowski and A.E. Young (1977). Dynamics of ionic composition of cerebral interstitial fluid in acute metabolic acid-base disturbances. Proc. Internat. Union Physiol. Sci. 13: 223.

Fencl, V., T.B. Miller and J.R. Pappenheimer (1966). Studies on the respiratory response to disturbances of acid-base balance, with deductions concerning the ionic composition of cerebral interstitial fluid. Am. J. Physiol. 210: 459-472.

Fencl, V., J.R. Vale and J.A. Broch (1969). Respiration and cerebral blood flow in metabolic acidosis and alkalosis in humans. J. Appl. Physiol. 27: 67-76.

Gabel, R.A. (1980). Algorithms for calculating and correcting blood-gas and acid-base variables. Respir. Physiol. 42: 211-232.

Javaheri, S., A. Clendening, N. Papadakis and J.S. Brody (1981). Change in brain surface pH during acute isocapnic metabolic acidosis. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 51: 276-281.

Javaheri, S., L. Herrera and H. Kazemi (1979). Ventilatory drive in acute metabolic acidosis. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 45: 913-918.

Kaehny, W.D. and J.T. Jackson (1979). Respiratory response to HCl acidosis in dogs after carotid body denervation. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 46: 1138-1142.

Katsaros, B. (1965). Die Rolle der Chemoreceptoren des Carotisgebiets der narkotisierten Katze für die Antwort der Atmung auf isolierte Änderung der Wasserstoffionen-Konzentration und des CO_2-Drucks des Blutes. Pflügers Arch. 282: 157-178.

Loeschcke, H.H. and H.R. Ahmad (1982). Fast bicarbonate-chloride exchange between plasma and brain extracellular fluid at maintained PCO_2. Pflügers Arch. 295: 300-305.

Miller, M.J. and S.M. Tenney (1975). Hyperoxic hyperventilation in carotid-deafferented cats. Respir. Physiol. 23: 23-30.

Mitchell, R.A. (1965). The regulation of respiration in metabolic acidosis and alkalosis. In: Cerebrospinal Fluid and the Regulation of Ventilation, edited by C. McC. Brooks, F.F. Kao, and B.B. Lloyd. Oxford: Blackwell, pp. 109-131.

Mitchell, R.A., D.A. Herbert and C.T. Carman (1965). Acid-base constants and temperature coefficients for cerebrospinal fluid. J. Appl. Physiol. 20: 27-30.

Mitchell, R.A., H.H. Loeschcke, W.H. Massion and J.W. Severinghaus (1963). Respiratory responses mediated through superficial chemosensitive areas of the medulla. J. Appl. Physiol. 18: 523-533.

Pappenheimer, J.R. (1967). The ionic composition of cerebral extracellular fluid and its relation to control of breathing. Harvey Lect. 6: 71-93.

Ponte, J. and M.J. Purves (1974). The role of the carotid body chemoreceptors and carotid sinus baroreceptors in the control of cerebral blood vessels. J. Physiol., London. 237: 315-340.

Pontén, U. and B.K. Siesjö (1966). Gradients of CO_2 tension in the brain. Acta Physiol. Scand. 67: 129-140.

Read, D.J.C. (1967). A clinical method for assessing the ventilatory response to carbon dioxide. Australas. Ann. Med. 16: 20-32.

Robin, E.D., R.D. Whaley, C.H. Crump, A.G. Bickelmann and D.M. Travis (1958). Acid-base relations between spinal fluid and arterial blood with special reference to control of ventilation. J. Appl. Physiol. 13: 385-392.

Severinghaus, J.W. (1966). Blood gas calculator. J. Appl. Physiol. 21: 1108-1116.

Steinbrook, R.A., J.C. Donovan, R.A. Gabel, D.E. Leith and V. Fencl (1983). Acclimatization to high altitude in goats with ablated carotid bodies. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. (in press).

Tenney, S.M. and J.G. Brooks (1966). Carotid bodies, stimulus interaction, and ventilatory control in unanesthetized goats. Respir. Physiol. 1:211-224.

Vatner, S.F., L.L. Priano, J.D. Rutherford and W.T. Manders (1980). Sympathetic regulation of the cerebral circulation by the carotid chemoreceptor reflex. Am. J. Physiol. 238: H594-H598.

TABLE 1

Effects of ablation of the carotid bodies and of acute metabolic acidosis on composition of arterial blood and CSF.

	Arterial Blood						CSF			
	pH	PCO_2 torr	PO_2 torr	BE meq/L	$[HCO_3^-]$ mmol/L	$[Cl^-]$ mmol/L	pH	PCO_2 torr	$[HCO_3^-]$ mmol/L	$[Cl^-]$ mmol/L
CB intact										
Control	7.423±0.005	37.1±1.0	93±1	-0.3±0.5	23.7±0.5	112±2	7.306±0.013	44.4±1.2	23.7±0.4	132±1
AMA	7.284±0.023	33.0±0.9	95±3	-10.1±1.4	15.4±1.2	123±2	7.308±0.004	38.8±1.0	22.8±0.3	134±3
CB ablated										
Control	7.399±0.004	39.7±0.8	86±2	-0.7±0.7	23.6±0.6	112±1	7.307±0.011	44.6±0.6	24.8±0.5	130±1
AMA	7.286±0.013	35.7±1.3	91±2	-9.0±0.9	16.2±0.8	120±2	7.306±0.015	41.6±0.6	23.6±0.2	131±1
Analysis of variance:										
Effect of CBx on variables during control periods:										
p	<0.05	<0.05	<0.05	NS	NS	NS	NS	NS	NS	NS
Effect of CBx on variables during AMA:										
p	NS	NS	NS	NS	NS	NS	NS	<0.05	NS	NS
AMA vs Control, CB intact:										
p	<0.005	<0.05	NS	<0.005	<0.001	<0.01	NS	<0.05	<0.05	NS
AMA vs Control, CBx:										
p	<0.005	<0.05	<0.05	<0.005	<0.001	<0.01	NS	<0.05	<0.05	NS

Values are means ± S.E. of repeated measurements in 4 goats. CB: carotid bodies; CBx: ablated CB; Control: normal metabolic acid-base balance; AMA: acute metabolic acidosis.

TABLE 2

Ventilatory response to hyperoxic CO_2 rebreathing of awake goats.

	$\dot{V}_E$ at P_{ETCO_2} = 60 torr L/min, BTPS	Slope of CO_2 response curves L/(min x torr)
Carotid bodies intact		
Control	29.5 ± 6.7	3.5 ± 0.4
AMA	43.0 ± 7.3*	3.6 ± 0.1
Carotid bodies ablated		
Control	17.3 ± 2.6†	2.9 ± 0.3
AMA	23.8 ± 3.6*†	3.2 ± 0.3

Analysis of variance:

* AMA significantly different from control ($p < 0.05$).

† Significantly different from the value with carotid bodies intact ($p < 0.05$).

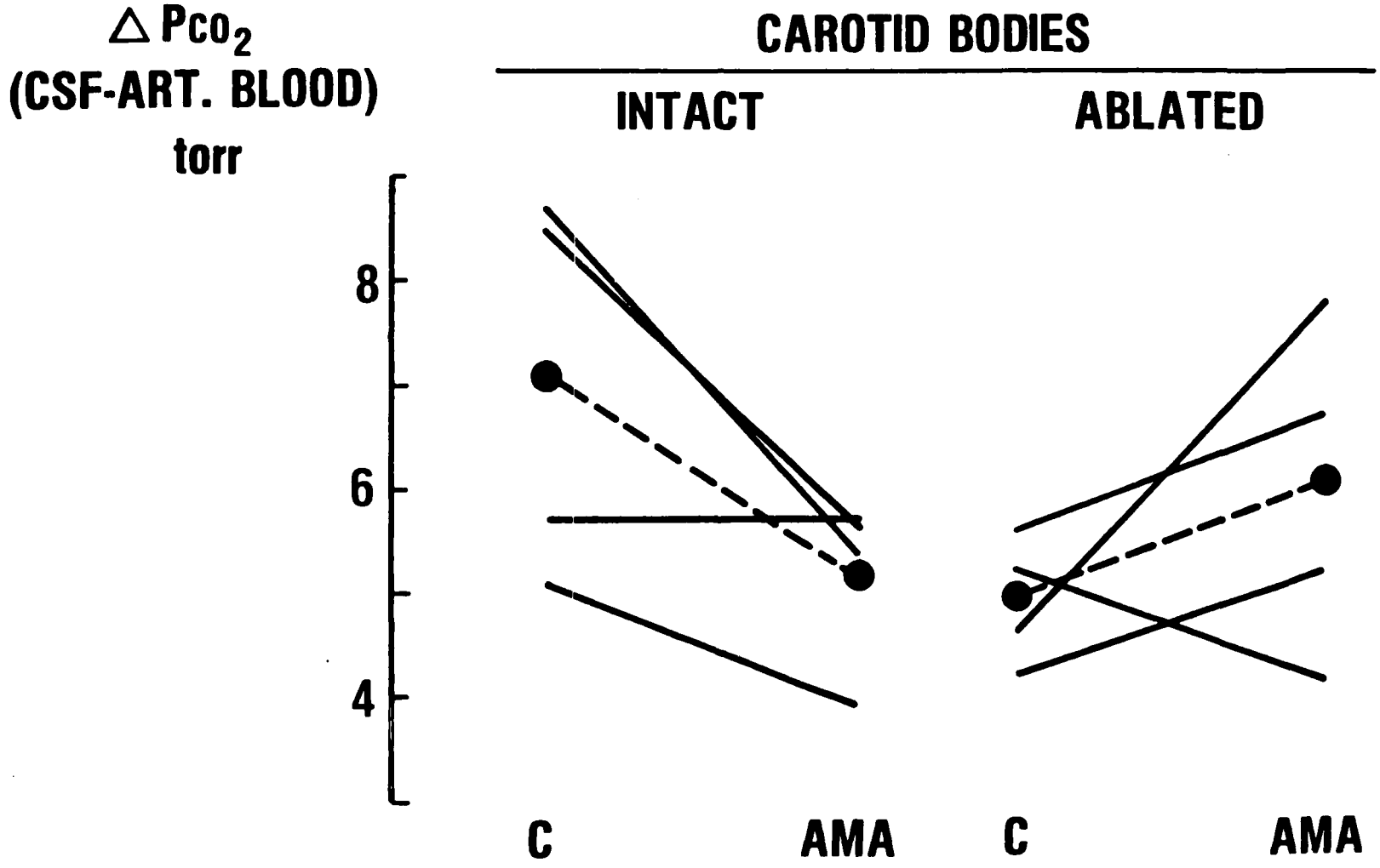
Values are means ± S.E. of repeated measurements in 4 goats (P_aO_2 > 300 torr).

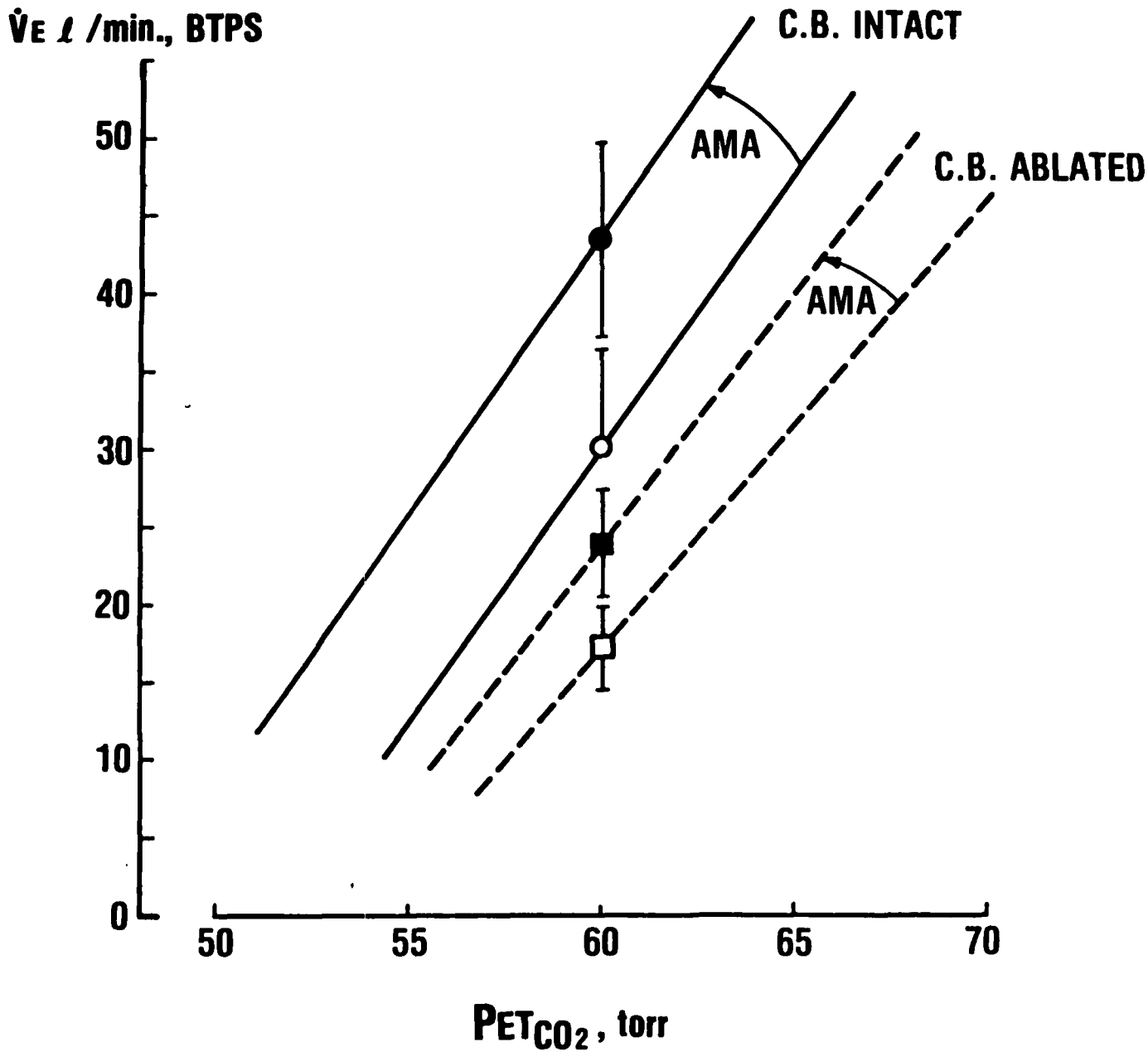
Control: normal metabolic acid-base balance; AMA: acute metabolic acidosis (base deficit 9 to 10 meq/L).

LEGENDS TO FIGURES

Figure 1. Effect of acute metabolic acidosis (AMA) on the difference in PCO_2 between cisternal CSF and arterial blood in goats with intact and ablated carotid bodies. The points joined by a broken line indicate mean values. C: Control (normal metabolic acid-base balance).

Figure 2. Effect of ablation of carotid bodies (C.B.) and of acute metabolic acidosis (AMA) on ventilatory responses to hyperoxic CO_2 rebreathing (PaO_2 > 300 torr). Constructed from mean values of $\dot{V}_E$ at $P_{ET}CO_2$ = 60 torr, and from mean values of slopes of the plots $\dot{V}_E$ vs $P_{ET}CO_2$. See Table 2 for numerical data. Open symbols: mean (± S.E.) values of $\dot{V}_E$ at $P_{ET}CO_2$ = 60 torr in normal metabolic acid-base balance. Closed symbols apply to AMA.


△ Pco2
(CSF-ART. BLOOD)
torr
CAROTID BODIES
INTACT
ABLATED
8
6
4
C
AMA
C
AMA


V̇E ℓ /min., BTPS
C.B. INTACT
AMA
C.B. ABLATED
AMA
50
40
30
20
10
0
50
55
60
65
70
PETCO2, torr

ANIMAL RESEARCH

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," as prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council.

The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other official documentation.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